

Fig. 1A

1st Round : screening of mutants (full length Ala-scan)

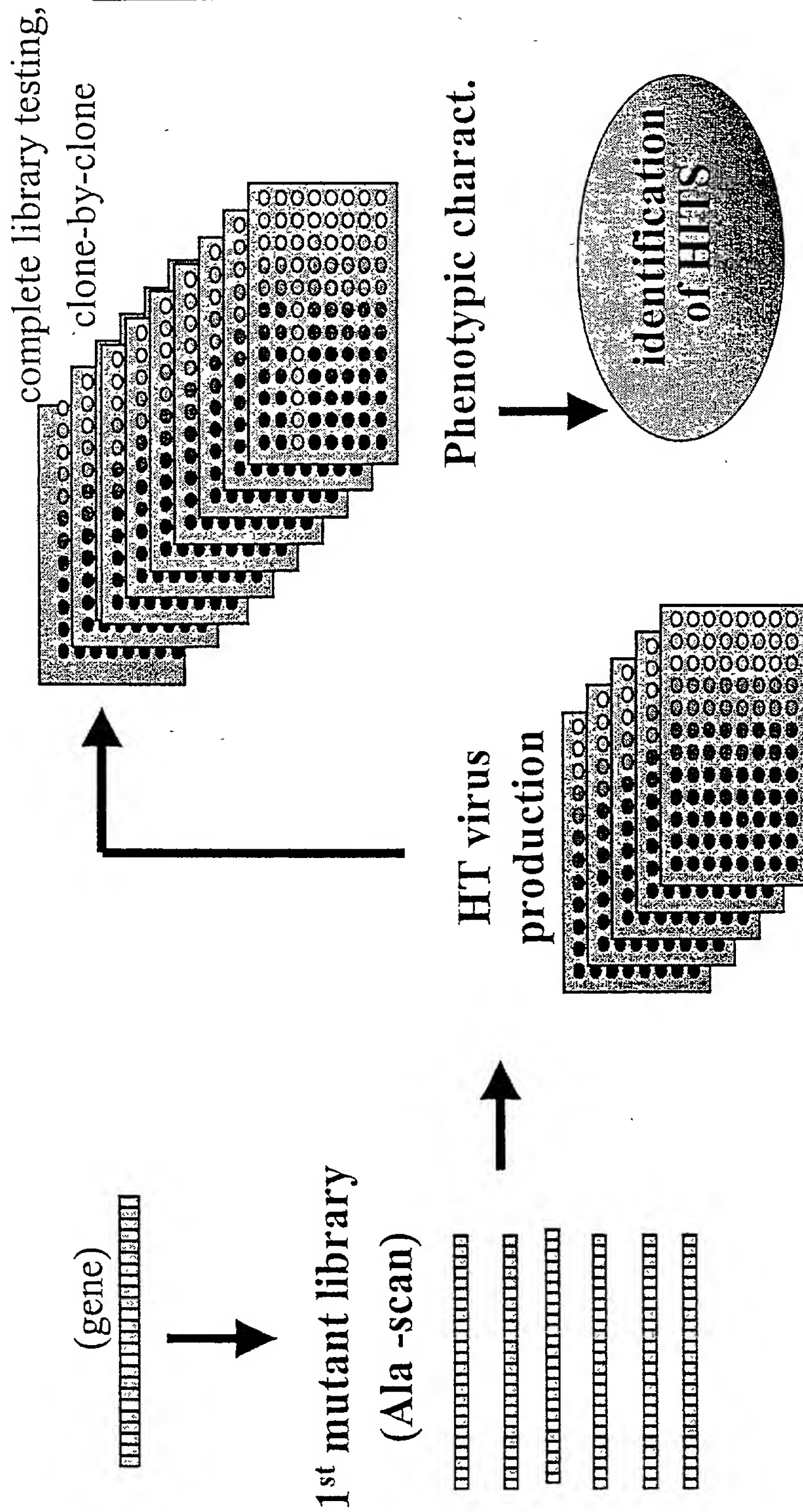
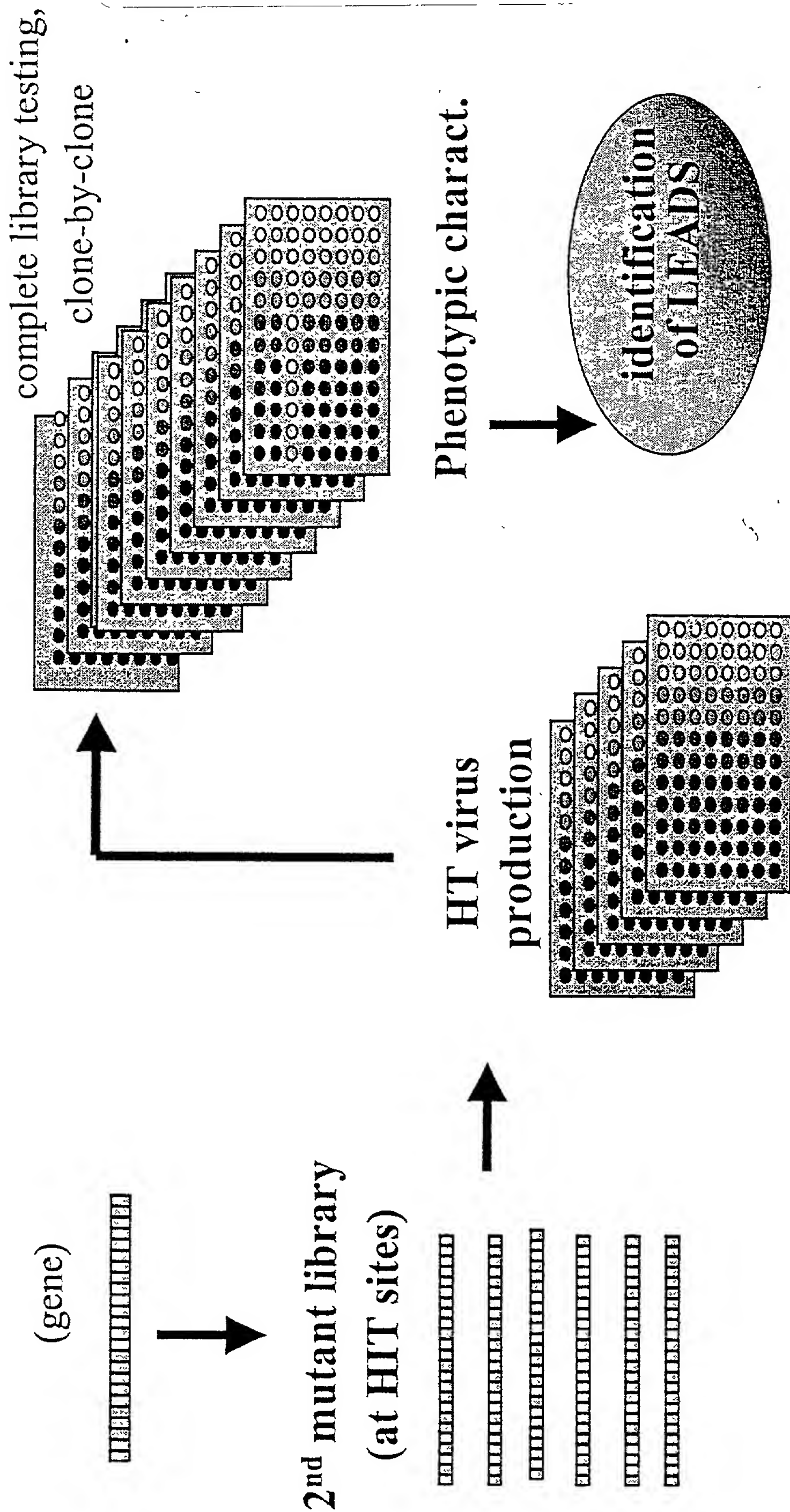


FIG. 1B

2nd Round : screening of mutants at (surrounding) HIT positions



TO/TT 642200T

F16.1C

3rd Round : screening of recombinants between LEADS

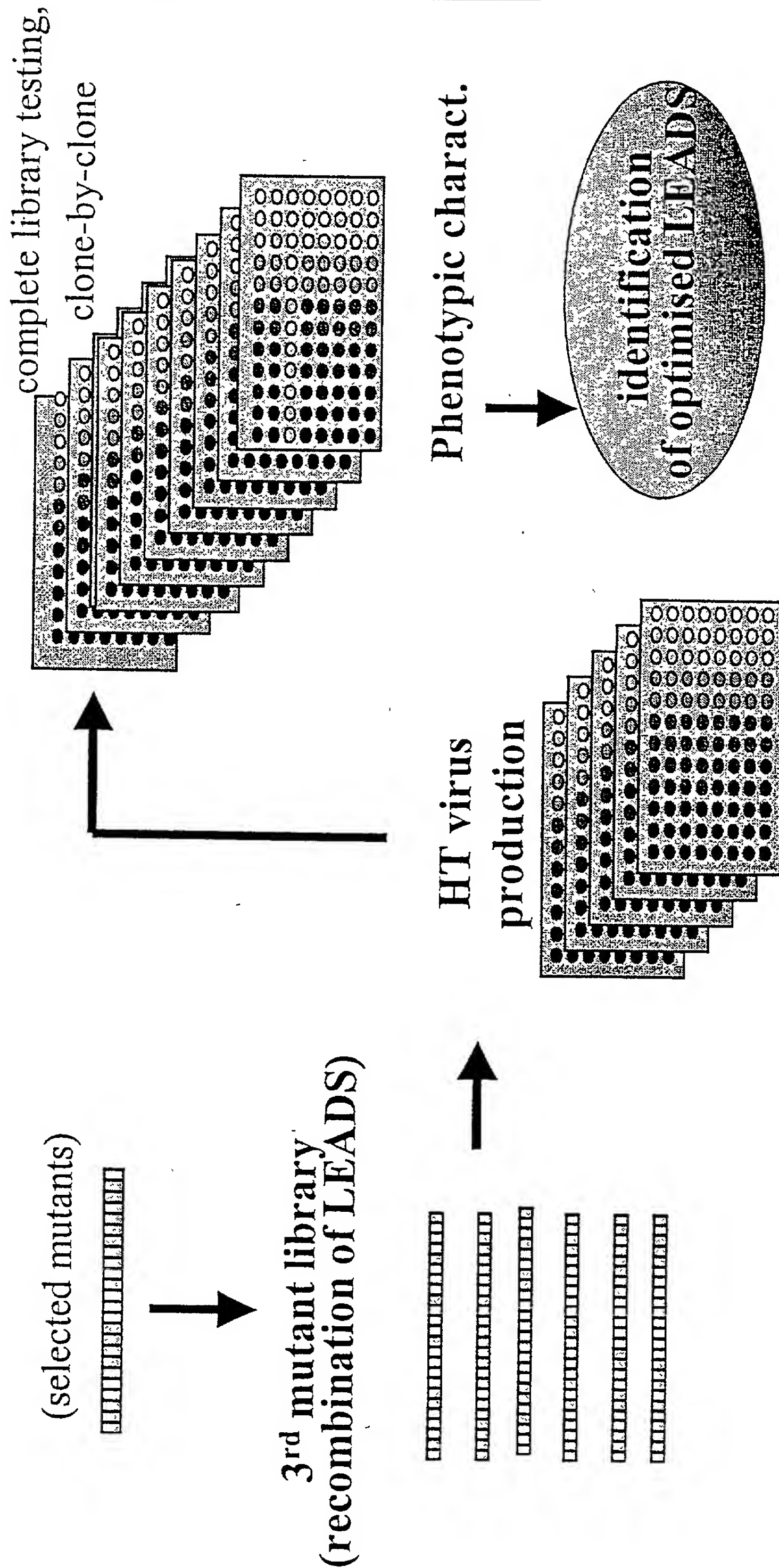
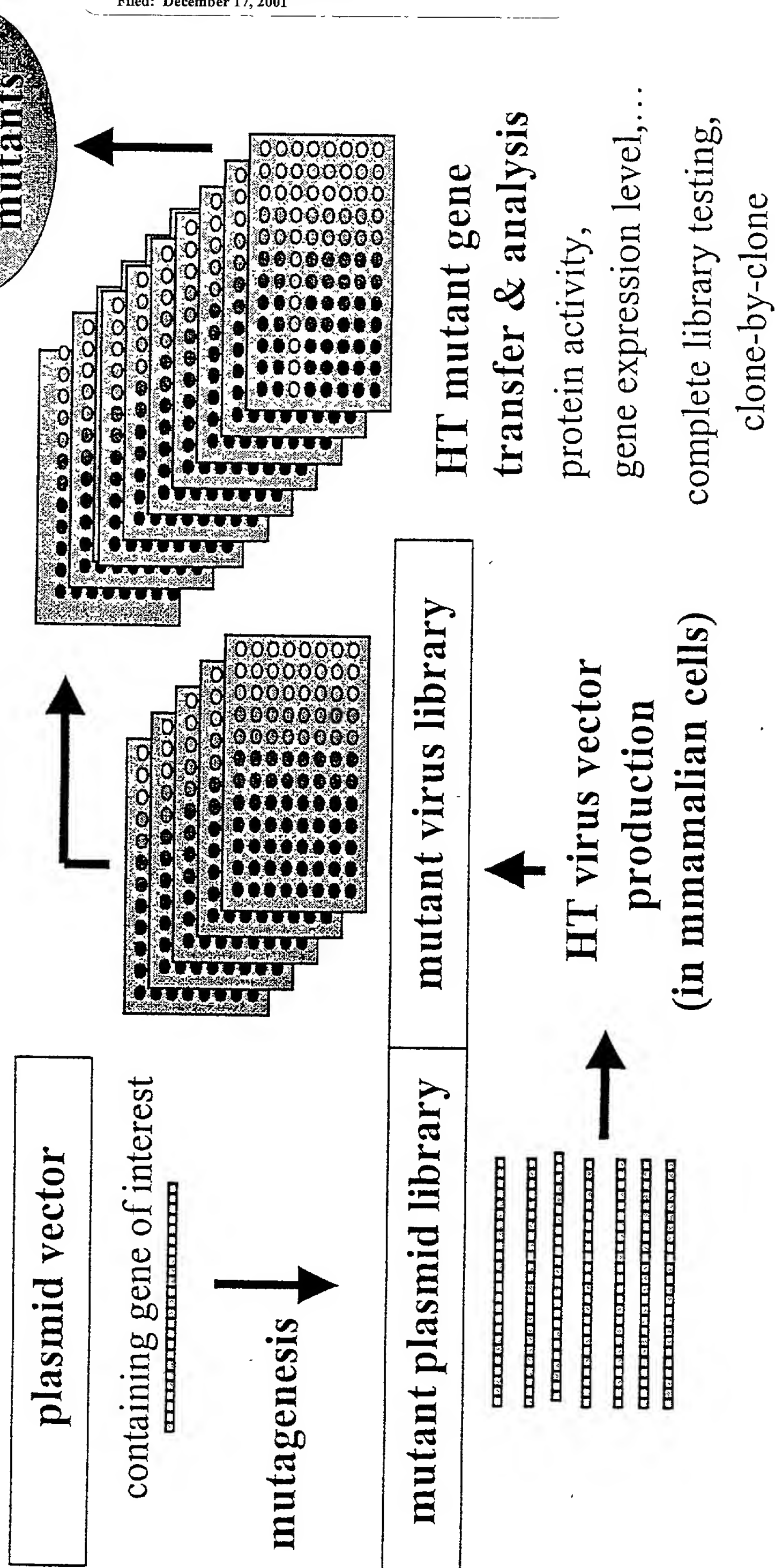


FIG. 1D

Gene optimisation (in mamalian cells)



F-16. 1E

Gene optimisation (in bacteria)

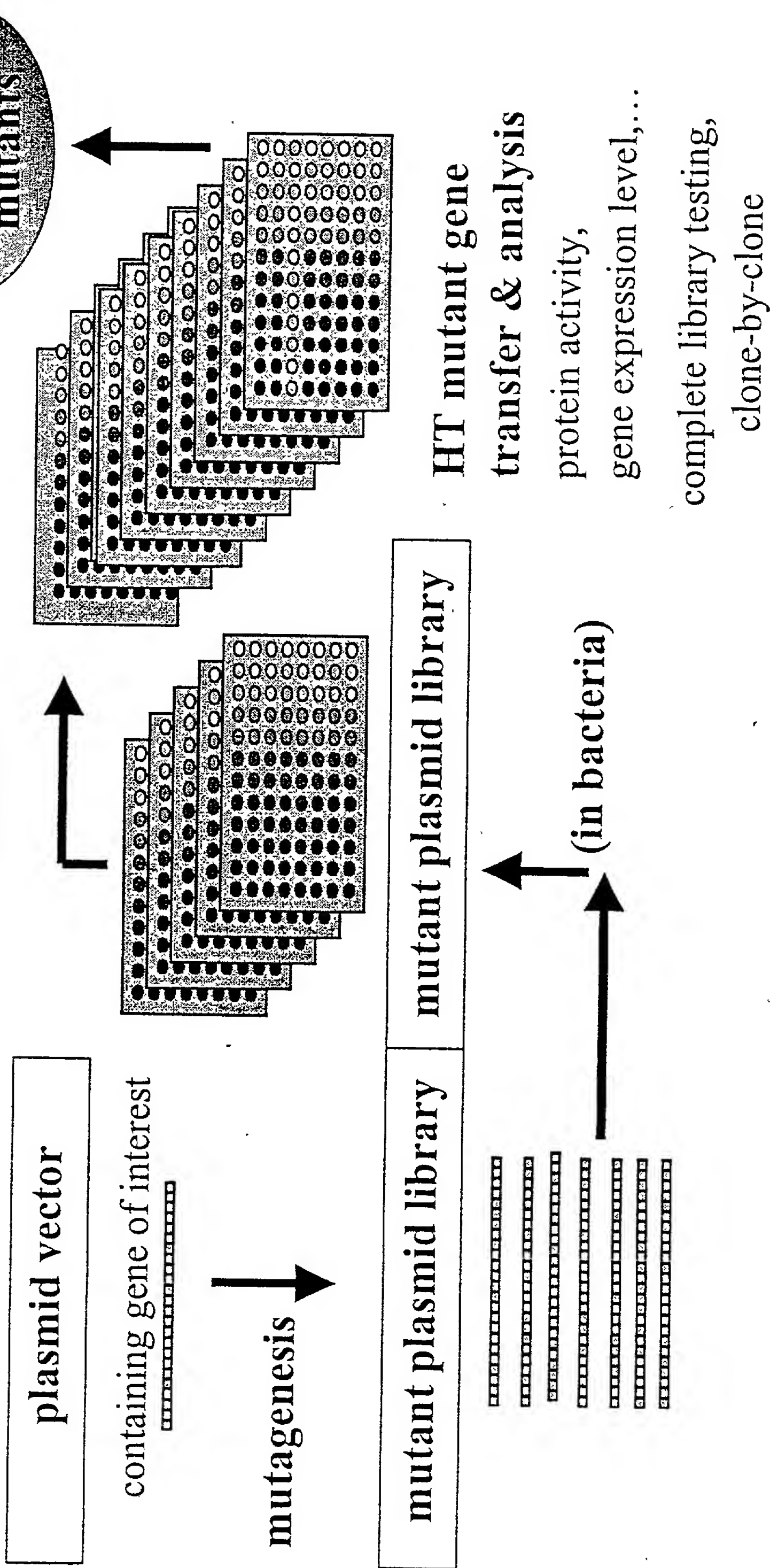


FIG. 2A

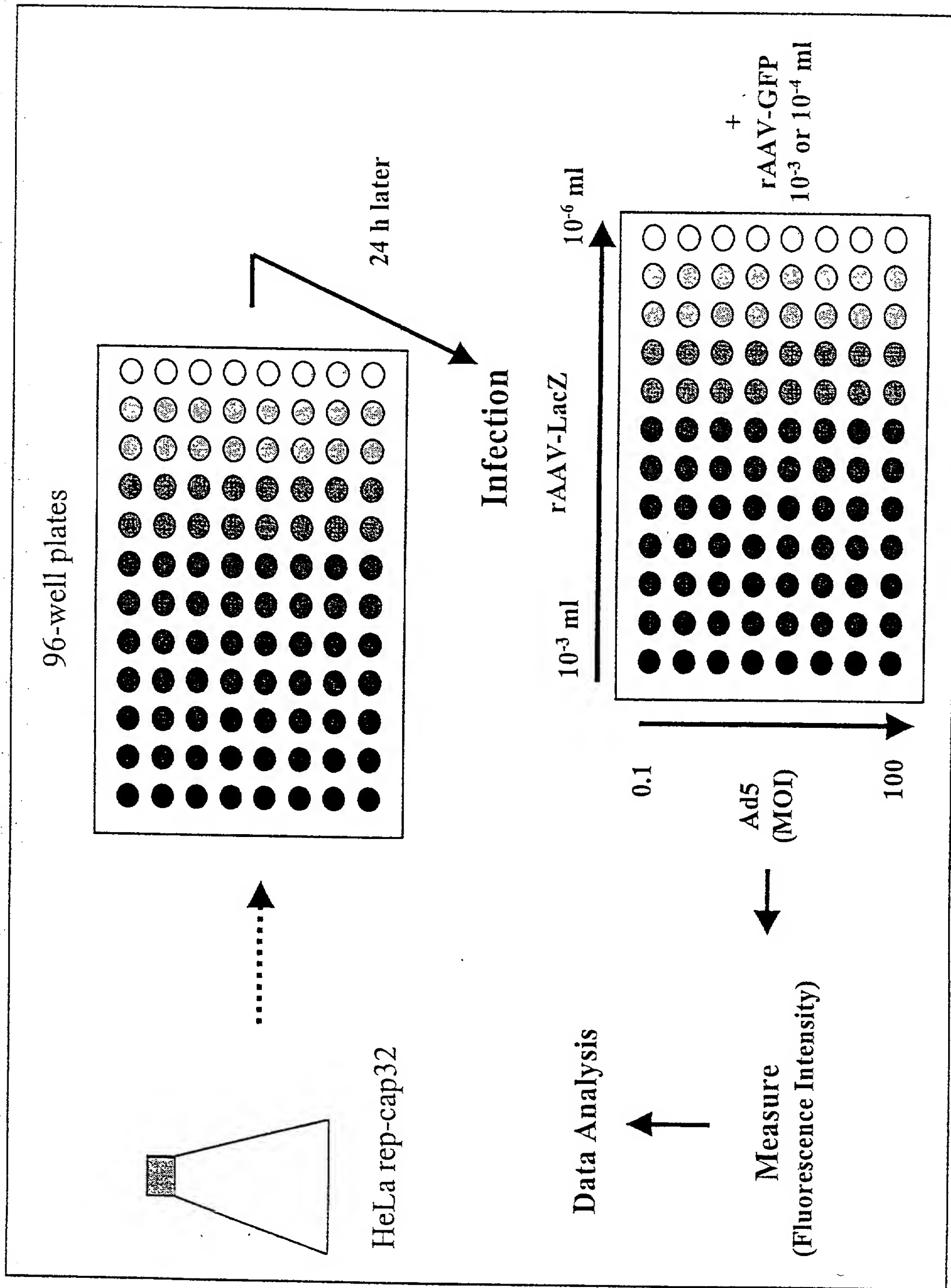


FIG 7B

TREE AAV lacZ 1 μ l+AAV GFP 1 μ l

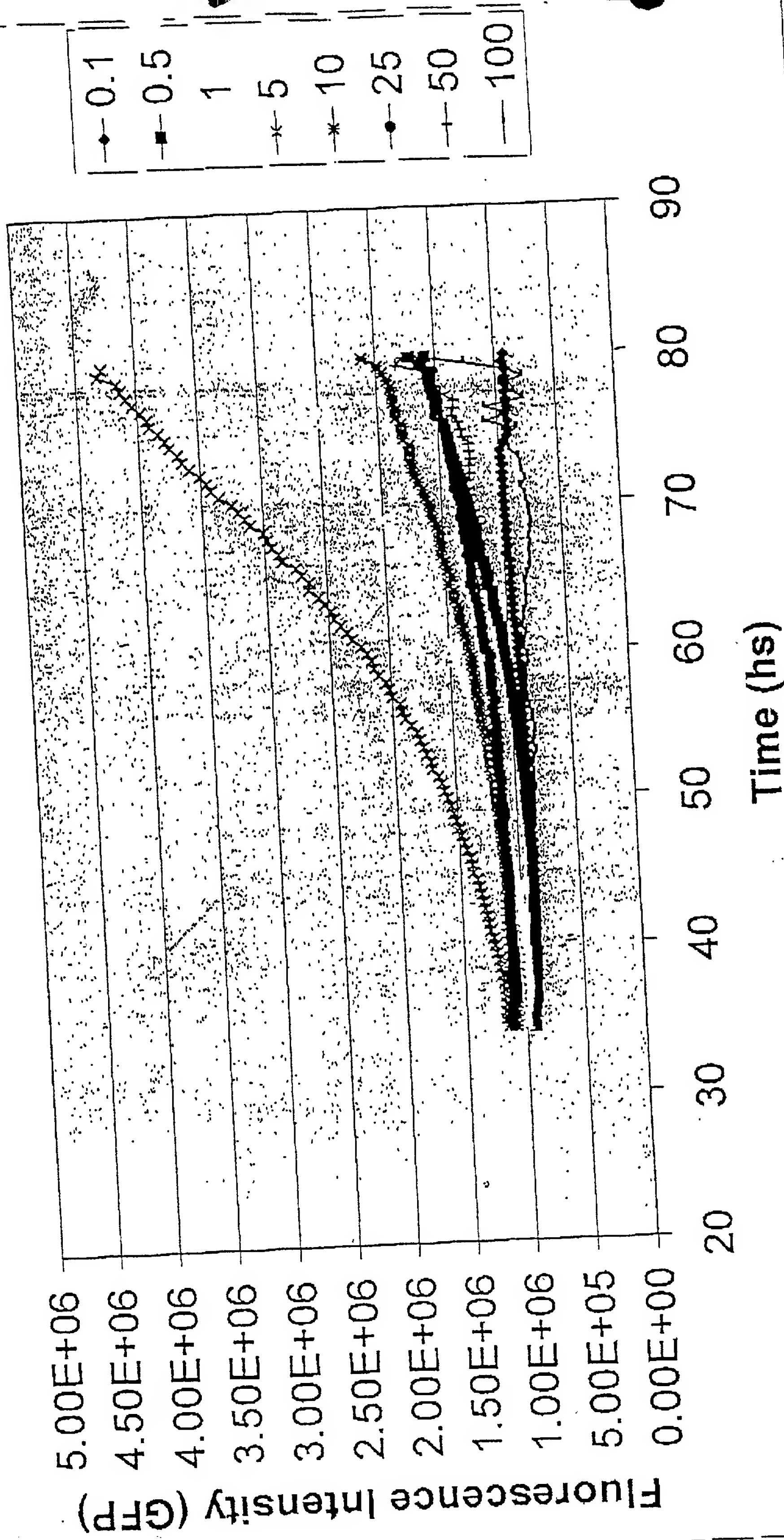


FIG. 2C

Figure N° 2C Quantification of unknown AAV infectious particles by
TREE

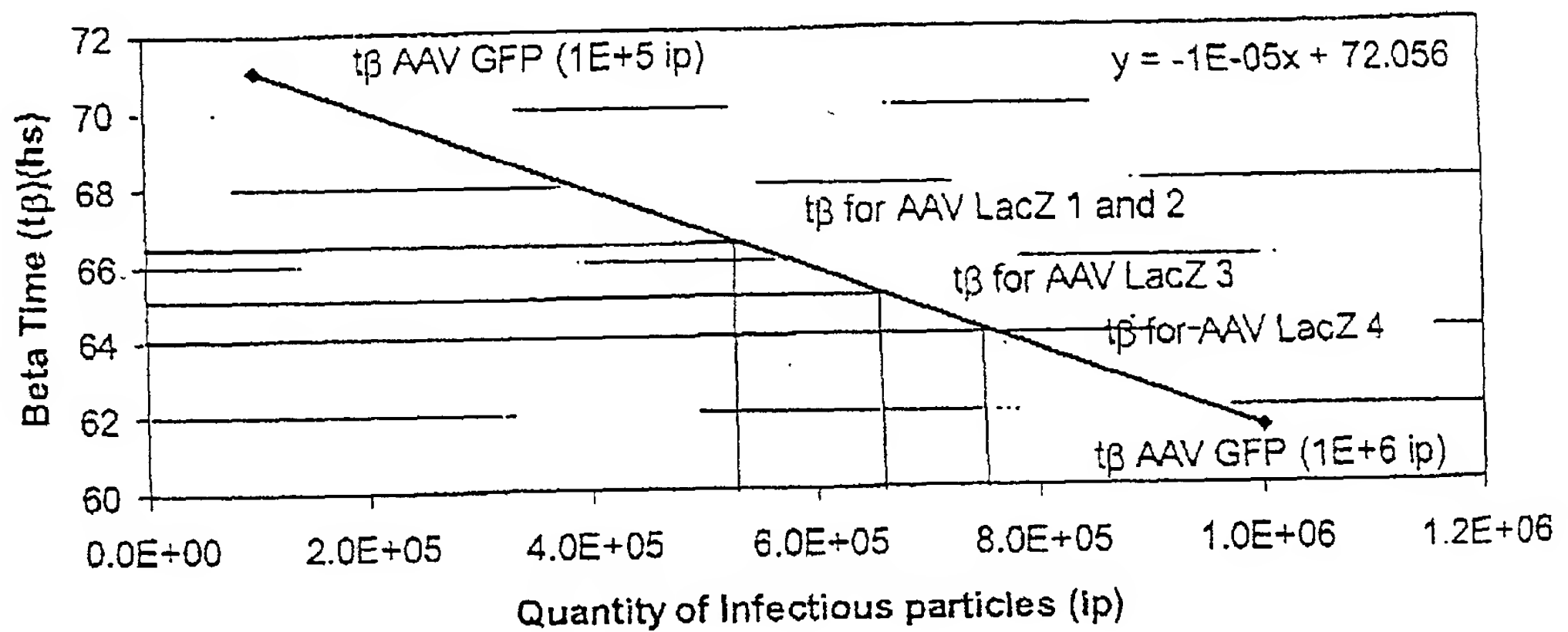


FIGURE 3A

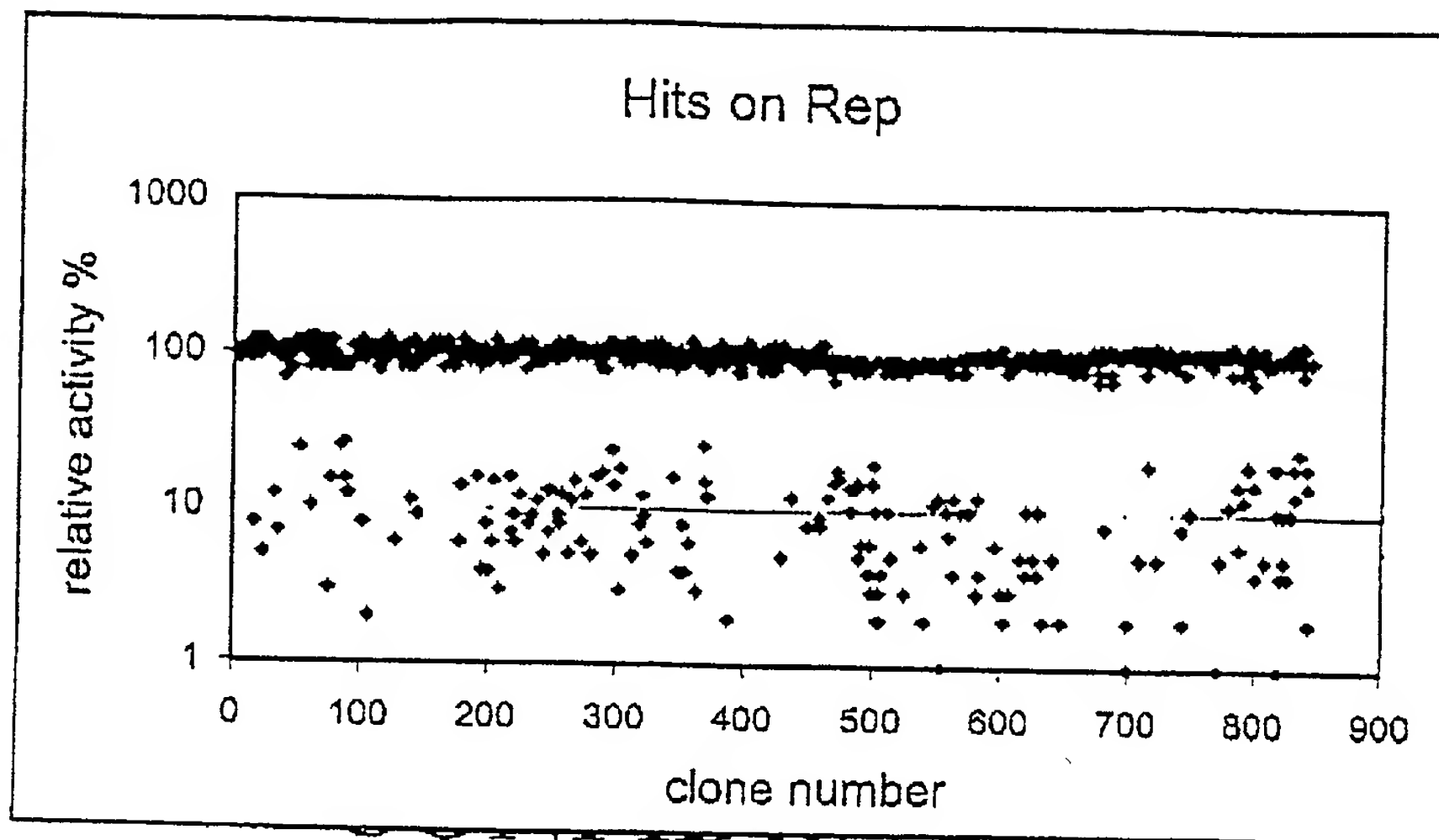


FIGURE 3B

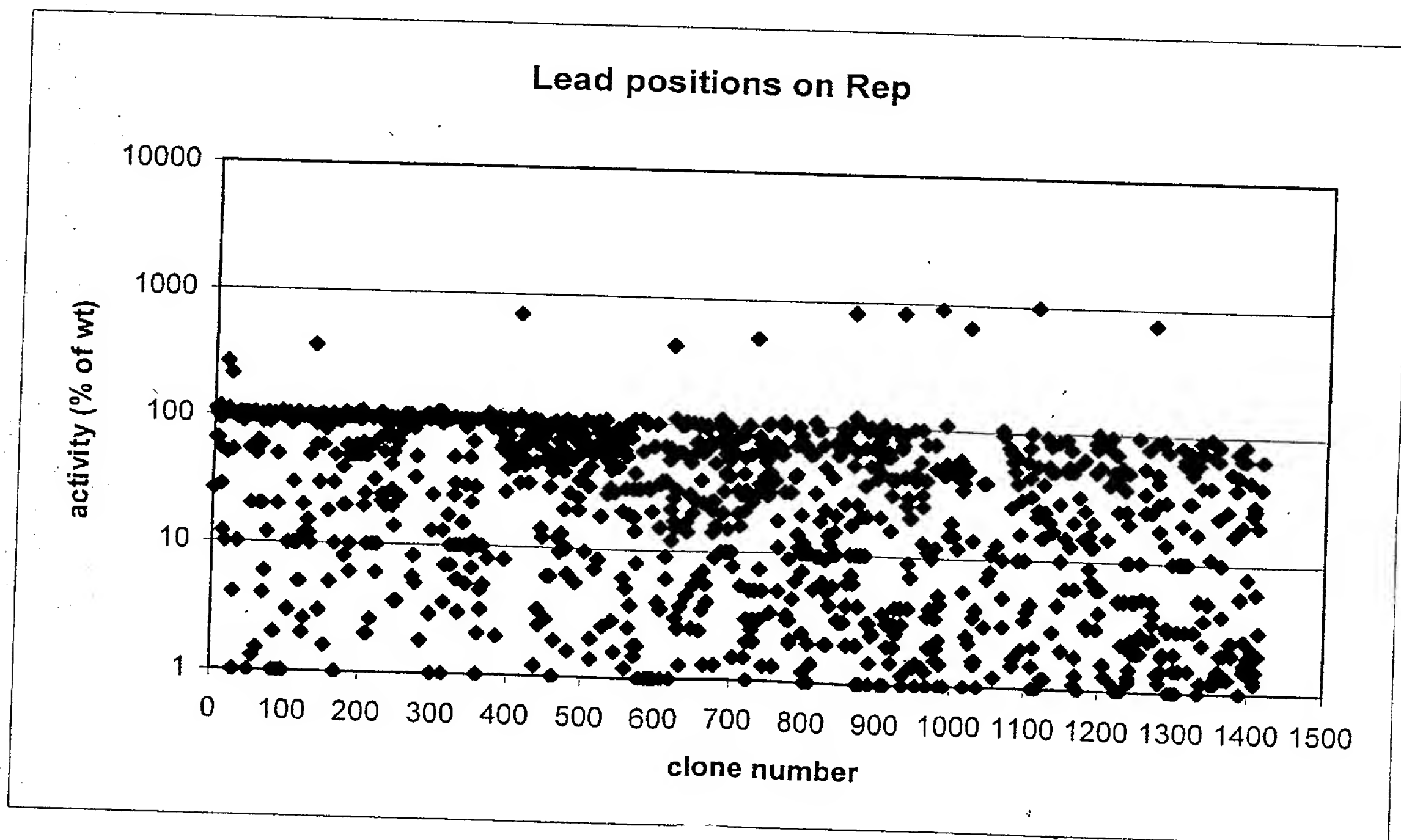
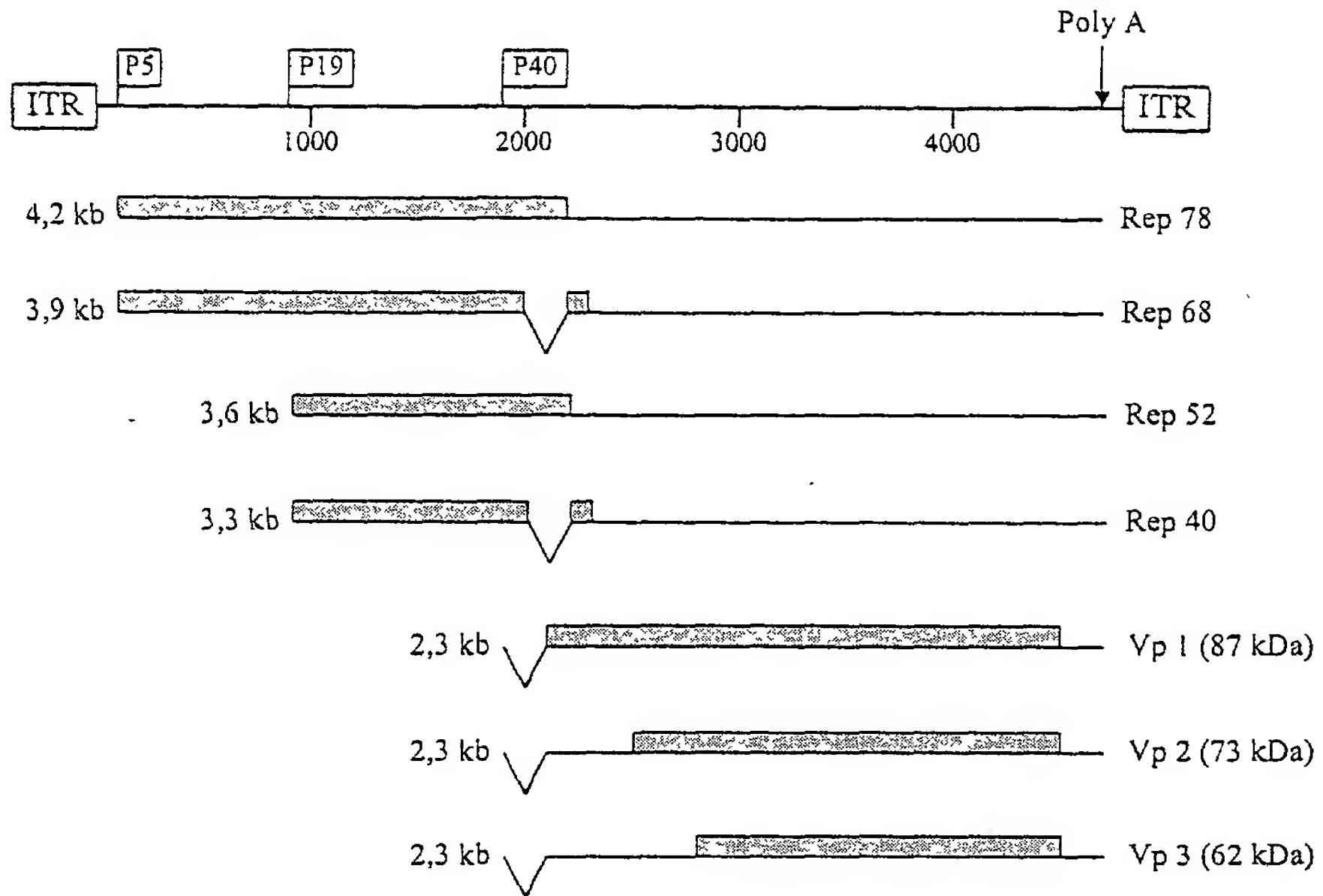


FIGURE 4



	10	20	30	40	50	60	
1	MPG	FYEIVIKVPSDLDEHLPGISDSFVSWVAEKEWELPPDSMDLNLIEQAPLTVAEKLQ	60				
2	MPG	FYEIVIKVPSDLDEHLPGISDSFVNWVAEKEWELPPDSMDLNLIEQAPLTVAEKLQ	60				
3	MPG	FYEIVLKVPSDLDEHLPGISNSFVNWVAEKEWELPPDSMDPNLIEQAPLTVAEKLQ	60				
4	MPG	FYEIVLKVPSDLDEHLPGISNSFVNWVAEKEWELPPDSMDPNLIEQAPLTVAEKLQ	60				
5	MPG	FYEIVLKVPSDLDEHLPGISDSFVSWVAEKEWELPPDSMDLNLIEQAPLTVAEKLQ	60				
6	MPG	FYEIVIKVPSDLDEHLPGISDSFVNWVAEKEWELPPDSMDLNLIEQAPLTVAEKLQ	60				
7	MAT	FYEVIVRVPFDVEEHLPGISDSFVDWVTGQIWELPPESDLNLTLVEQPQLTVADRIR	60				
C	M**FYE**	:*VP*D***HLPGIS+SFV:WV****WELPP*SD**+*L*EQ**LTVA****					
	70	80	90	100	110	120	
1	RDF	LVQWRRVSKAPEALFFVQFEKGESYFHLHLVETTTGVKSMVLGRFLSQIRDKLVQTI	120				
2	RDF	LVQWRRVSKAPEALFFVQFEKGESYFHLHLVETTTGVKSMVLGRFLSQIRDKLVQTI	120				
3	REF	LVEWRRVSKAPEALFFVQFEKGETYFHLHLVLIETIGVKSMVVGGRYVSQIKEKLVTRI	120				
4	REF	LVEWRRVSKAPEALFFVQFEKGETYFHLHLVLIETIGVKSMVVGGRYVSQIKEKLVTRI	120				
5	REF	LVEWRRVSKAPEALFFVQFEKGDSYFHLHLVETTVGVKSMVVGGRYVSQIKEKLVTRI	120				
6	RDF	LTEWRRVSKAPEALFFVQFEKGESYFHMHLVETTTGVKSMVLGRFLSQIREKLIQRI	120				
7	RVF	LYEWNKFSKQ-ESKFFVQFEKGSEYFHLHTLVETSGISSMVLGRYVSQIRAOQLVKVV	119				
C	R:FL++W***SK**E**FFVQFEKG+	:YFH*H:L+ET:G**SMV:GR::SQI::*L*::*					
	130	140	150	160	170	180	
1	YRG	IEPTLPNWF	AVTKTRNGAGGGNKVVDECYIPNYLLPKTQPELQWAWTNMEEYISACL	180			
2	YRG	IEPTLPNWF	AVTKTRNGAGGGNKVVDECYIPNYLLPKTQPELQWAWTNMEEYISACL	180			
3	YRG	VEPQLPNWF	AVTKTRNGAGGGNKVVDDCYIPNYLLPKTQPELQWAWTNMDQYLSACL	180			
4	YRG	VEPQLPNWF	AVTKTRNGAGGGNKVVDDCYIPNYLLPKTQPELQWAWTNMDQYLSACL	180			
5	YRG	VEPQLPNWF	AVTKTRNGAGGGNKVVDDCYIPNYLLPKTQPELQWAWTNMDQYISACL	180			
6	YRG	IEPTLPNWF	AVTKTRNGAGGGNKVVDECYIPNYLLPKTQPELQWAWTNMEQYLSACL	180			
7	FQGI	EPQINDWVAITKVKK--GGANKVVDSGYIPAYLLPKVQPELQWAWTNLDEYKLAAL	177				
C	**G:EP:***W*A*TK*****GG*NKVV	:*YIP*YLLPK*QPELQWAWTN*::Y:*A*L					
	190	200	210	220	230	240	
1	NLA	ERKRLVAQHLTHVSQTQEONKENLNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK	240				
2	NLA	ERKRLVAHDLTHVSQTQEONKENLNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK	240				
3	NLA	ERKRLVAQHLTHVSQTQEONKENQNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK	240				
4	NLA	ERKRLVAQHLTHVSQTQEONKENQNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK	240				
5	NLA	ERKRLVAQHLTHVSQTQEONKENQNPNSDAPVIRSKTSARYMELVGWLVDRGITSEK	240				
6	NL	TERKRLVAQHLTHVSQTQEONKENQNPNSDAPVIRSKTSARYMELVGWLVDKGITSEK	240				
7	NLE	ERKRLVAQFLAESSQRS-QEAASQREFSADPVIKSKTSQKYMALVNWLVEHGITSEK	236				
C	NL+ERKRLVA*+L***SQ***Q****+***S**PVI*SKTS**YM*LV*WLV*+GITSEK						
	250	260	270	280	290	300	
1	QWI	QEDQASYISFNAASNSRSQIKAALDNAGKIMALT	KSAPDYL	VGPAPPADIKTNRIYR	300		
2	QWI	QEDQASYISFNAASNSRSQIKAALDNAGKIMALT	KSAPDYL	VGPAPPADIKTNRIYR	300		
3	QWI	QEDQASYISFNAASNSRSQIKAALDNASKIMSLTKTAPDYL	VGSNPPEDITKNRIYQ	300			
4	QWI	QEDQASYISFNAASNSRSQIKAALDNASKIMSLTKTAPDYL	VGSNPPEDITKNRIYQ	300			
5	QWI	QEDQASYISFNAASNSRSQIKAALDNASKIMSLTKTAPDYL	VGQNPPEDISSNRIYR	300			
6	QWI	QEDQASYISFNAASNSRSQIKAALDNAGKIMSLTKTAPDYL	VGQQPVEDISSNRIYK	300			
7	QWI	QENQESYLSFNSTGNSRSQIKAALDNATKIMSLTKSAVDYL	VGSSVPEDISKNIWQ	296			
C	QWIQE*Q*SY*SFN***NSRSQIKAALDNA:KIM+LTK:A*DYL	VG::**+DI::NRI*:					
	310	320	330	340	350	360	
1	I	LELNGYEPAYAGSVFLGWAQKRFGKRNTIWLFGPATTGKT	NIAEAI	AHAVPFYGCVNWT	360		
2	I	LELNGYDPAYAGSVFLGWAQKRFGKRNTIWLFGPATTGKT	NIAEAI	AHAVPFYGCVNWT	360		
3	I	LELNGYDPQYAASVFLGWAQKKFGKRNTIWLFGPATTGKT	NIAEAI	AHAVPFYGCVNWT	360		
4	I	LELNGYDPQYAASVFLGWAQKKFGKRNTIWLFGPATTGKT	NIAEAI	AHAVPFYGCVNWT	360		
5	I	LEMNGYDPQYAASVFLGWAQKKFGKRNTIWLFGPATTGKT	NIAEAI	AHAVPFYGCVNWT	360		
6	I	LELNGYDPQYAASVFLGWATKKFGKRNTIWLFGPATTGKT	NIAEAI	AHTVPFYGCVNWT	360		
7	I	FEMNGYDPAYAGSILYGWCQRSFNKRNTVWLYGPATTGKT	NIAEAI	AHTVPFYGCVNWT	356		

FIGURE 5B

370 380 390 400 410 420
1 NENFPFND CVDK MVIW WEEG KMTAKV VESAKAILGGSKVRVDQKCKSSAQIDPTPVIVTS 420
2 NENFPFND CVDK MVIW WEEG KMTAKV VESAKAILGGSKVRVDQKCKSSAQIDPTPVIVTS 420
3 NENFPFND CVDK MVIW WEEG KMTAKV VESAKAILGGSKVRVDQKCKSSAQIEPTPVIVTS 420
4 NENFPFND CVDK MVIW WEEG KMTAKV VESAKAILGGSKVRVDQKCKSSAQIEPTPVIVTS 420
5 NENFPFND CVDK MVIW WEEG KMTAKV VESAKAILGGSKVRVDQKCKSSAQIDPTPVIVTS 420
6 NENFPFND CVDK MVIW WEEG KMTAKV VESAKAILGGSKVRVDQKCKSSAQIDPTPVIVTS 420
7 NENFPFND CVDK MLIW WEEG KMTNKV VESAKAILGGSKVRVDQKCKSSVQIDSTPVIVTS 416
C NENFPFND CVDK M*IW WEEG KMT*KV VESAKAILGGSKVRVDQKCKSS*QI+*TPVIVTS

430 440 450 460 470 480
1 NTNMC AVIDGNSTTFEHQQPLQDRMFKFELTRRLDHDGKVTQKEVKDFFRWASDHVTEV 480
2 NTNMC AVIDGNSTTFEHQQPLQDRMFKFELTRRLDHDGKVTQKEVKDFFRWASDHVTEV 480
3 NTNMC AVIDGNSTTFEHQQPLQDRMFKFELTRRLDHDGKVTQKEVKDFFRWASDHVTEV 480
4 NTNMC AVIDGNSTTFEHQQPLQDRMFKFELTRRLDHDGKVTQKEVKDFFRWASDHVTEV 480
5 NTNMC AVIDGNSTTFEHQQPLQDRMFKFELTRRLDHDGKVTQKEVKDFFRWASDHVTEV 480
6 NTNMC AVIDGNSTTFEHQQPLQDRMFKFELTRRLDHDGKVTQKEVKDFFRWAKDHVVEV 480
7 NTNMC VVDGNSTTFEHQQPLEDRMFKFELTKRLPPDFGKITQKEVKDFFAWAKVNQVPV 476
C NTNMC*V* DGNSTTFEHQQPL*DRMFKFELT+RL: *DFGK*TKQEVK+FF*WA: ***+:V

490 500 510 520
1 AHEFYVRKGGANKRPAPDDADKSEPKRA-----CPSVADPSTSDAEG 522
2 AHEFYVRKGGANKRPAPDDADKSEPKRA-----CPSVADPSTSDAEG 522
3 AHEFYVRKGGAKKR PASNDADVSEPKRQ-----CTSLAQPTTSDAEA 522
4 AHEFYVRKGGAKKR PASNDADVSEPKRQ-----CTSLAQPTTSDAEA 522
5 THEFYVRKGGARKRPAPNDADISEPKRA-----CPSVAQPSTSDAEA 522
6 EHEFYVKKGGAKKR PAPSADADISEPKRV-----RESVAQPSTSDAEA 522
7 THEFKVPRELAGTKGAEKSLKRPLGDVTNTSYKSLEKRARLSFVPETPRSSDVTVDPAPL 536
C :HEF*V+***A:***A:***.*****: +:***:***A*:

530 540 550 560 570 580
1 APVDFADRYQNKCSRHAGMLQMLFPCKTCERMNQNFNICFTHGTRDCSECFP--GVSESQ 580
2 APVDFADRYQNKCSRHAGMLQMLFPCKTCERMNQNFNICFTHGTRDCSECFP--GVSESQ 580
3 P-ADYADRYQNKCSRHVGMNLMFLFPCKTCERMNQISNVCFTHGQRDCGECFPGMSESQPV 581
4 P-ADYADRYQNKCSRHVGMNLMFLFPCKTCERMNQISNVCFTHGQRDCGECFPGMSESQPV 581
5 P-VDYADRYQNKCSRHVGMNLMFLPCRQCERMNQNVNIDICFTHGVMDCAECFP-VSESQPV 580
6 S-INYADRYQNKCSRHVGMNLMFLPCRQCERMNQNSNICFTHGQKDCLECFP--VSESQP 579
7 RPLNWN SRYDCKCDYHAQFDNISNKCDECEYLNRGKNGCICHNVTHCQICHG----- 588
C :::+:**RY**KC**H:***:*****C::CE**N*:*:C**H*:*:C.*C**...::+:::

590 600 610 620
1 PVVRKRTYRKLCAIHLLGRAPEIACSACDLVNVDLDDCVSEQ 623
2 PVVRKRTYRKLCAIHLLGRAPEIACSACDLVNVDLDDCVSEQ 623
3 SVVKKKTYQKLCPIHHILGRAPEIACSACDLANVDLDDCVSEQ 624
4 SVVKKKTYQKLCPIHHILGRAPEIACSACDLANVDLDDCVSEQ 624
5 SVVRKRTYQKLCPIHHIMGRAPEVACSACELANVDLDDCDMEQ 623
6 VSVVKKAYQKLCYIHHIMG-KVPDACTACDLVNVDLDDCIFEQ 621
7 -----IPPWEKENLSDFGDFDDANKEQ 610
C :+*:+:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*:*D*DD*:EQ